

**Amendment and Response**

Serial No.: 09/641,801

Confirmation No.: 5388

Filed: August 17, 2000

For: USE OF COLOSTRININ, CONSTITUENT PEPTIDES THEREOF, AND ANALOGS THEREOF FOR INDUCING CYTOKINES

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Page 3 of 13

amino acid sequences are compared using the Blastp program, version 2.0.9, of the BLAST 2 search algorithm, available on the worldwide web at [ncbi.nlm.nih.gov/gorf/b12.html](http://ncbi.nlm.nih.gov/gorf/b12.html).

B2 Preferably, the default values for all BLAST 2 search parameters are used, including matrix = BLOSUM62; open gap penalty = 11, extension gap penalty = 1, gap x\_dropoff = 50, expect = 10, wordsize = 3, and filter on. In the comparison of two amino acid sequences using the BLAST search algorithm, structural similarity is referred to as "identity." Preferably, an active analog of colostrinin or its constituent peptides has a structural similarity to colostrinin or one or more of its constituent peptides (preferably, one of SEQ ID NOs:1-30) of at least about 70% identity, more preferably, at least about 80% identity, and most preferably, at least about 90% identity.

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**In the Claims**

Please cancel claims 5, 10, 12 and 36, amend claims 1, 6, 11, 20-29 and 31-35, and add new claims 37-39. The new and amended claims are provided below in clean form. Per 37 C.F.R. §1.121, amended claims are also shown in Appendix A with notations to indicate changes made (for convenience, all pending claims, including those added hereby, are provided in Appendix A).

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B3 1. [AMENDED] A method of inducing a cytokine in a cell, the method comprising contacting the cell with an immunological regulator under conditions effective to induce a cytokine, wherein the immunological regulator comprises MQPPPLP (SEQ ID NO:1), an active analog thereof, and combinations thereof, wherein the active analog comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent structural similarity to SEQ ID NO:1.

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B4 6. [AMENDED] A method for modulating an immune response in a cell, the method comprising contacting the cell with an immunological regulator under conditions effective to induce a cytokine, wherein the immunological regulator comprises MQPPPLP (SEQ ID NO:1), an active analog thereof, and combinations thereof, wherein the active analog comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent structural similarity to SEQ ID NO:1.

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B5 11. [AMENDED] A method for modulating an immune response in a patient, the method comprising administering to the patient an immunological regulator under conditions effective to induce a cytokine, wherein the immunological regulator comprises MQPPPLP (SEQ ID NO:1), an active analog thereof, and combinations thereof, wherein the active analog comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent structural similarity to SEQ ID NO:1.

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B6 20. [AMENDED] A method for modulating leukocyte proliferation, the method comprising contacting leukocytes with a leukocyte regulator selected from the group of colostrinin, a constituent peptide thereof, an active analog thereof, and combinations thereof, under conditions effective to change the number of leukocyte; wherein the active analog comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent structural similarity to one or more constituent peptides of colostrinin, which are selected from the group of SEQ ID NO:1 through SEQ ID NO:34.

21. [AMENDED] The method of claim 20 wherein the leukocytes are present in a cell culture or an organism.

22. [AMENDED] The method of claim 20 wherein the leukocytes are mammalian cells.

23. [AMENDED] The method of claim 22 wherein the leukocytes are human cells.
24. [AMENDED] The method of claim 22 wherein the leukocytes are increased in number.
25. [AMENDED] The method of claim 24 wherein the leukocytes are differentiated.
26. [AMENDED] The method of claim 22 wherein the leukocyte regulator is a constituent peptide of colostrinin.
27. [AMENDED] The method of claim 26 wherein the leukocyte regulator is selected from the group of MQPPPLP (SEQ ID NO:1), LQTPQPLLQVMMEPQGD (SEQ ID NO:2), DQPPDVEKPDLPFQVQS (SEQ ID NO:3), LFFFLPVVNVLP (SEQ ID NO:4), DLEMPVLPVEPFPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), LKFPFKLKVEVFPFP (SEQ ID NO:8), VVMEV (SEQ ID NO:9), SEQP (SEQ ID NO:10), DKE (SEQ ID NO:11), FPPPK (SEQ ID NO:12), DSQPPV (SEQ ID NO:13), DPPPPQS (SEQ ID NO:14), SEEMP (SEQ ID NO:15), KYKLQPE (SEQ ID NO:16), VLPPNVG (SEQ ID NO:17), VYPFTGPIPN (SEQ ID NO:18), SLPQNILPL (SEQ ID NO:19), TQTPVVVPPF (SEQ ID NO:20), LQPEIMGVPKVKETMVPK (SEQ ID NO:21), HKEMPFPKYPVEPFTESQ (SEQ ID NO:22), SLTLTDVEKLHLPLPLVQ (SEQ ID NO:23), SWMHQPP (SEQ ID NO:24), QLPPTVMFP (SEQ ID NO:25), PQSVLS (SEQ ID NO:26), LSQPKVLPVPQKAVPQRDMPIQ (SEQ ID NO:27), AFLLYQE (SEQ ID NO:28), RGPFPILV (SEQ ID NO:29), ATFNRYQDDHGEEILKSL (SEQ ID NO:30), VESYVPLFP (SEQ ID NO:31), FLLYQEPVLGPVR (SEQ ID NO:32), LNF (SEQ ID NO:33), and MHQPPQPLPPTVMFP (SEQ ID NO:34), an active analog thereof, and combinations thereof; wherein the active analog comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent structural similarity to one or more

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Page 6 of 13

constituent peptides of colostrinin, which are selected from the group of SEQ ID NO:1 through SEQ ID NO:34.

28. [AMENDED] The method of claim 27 wherein the leukocyte regulator is selected from the group of MQPPPLP (SEQ ID NO:1), LQTPQPLLQVMMEPQGD (SEQ ID NO:2), DQPPDVEKPDQLQPFQVQS (SEQ ID NO:3), LFFFLPVVNVLP (SEQ ID NO:4), DLEMPVLPVEPFPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), LKPFPKLKVEVFPEP (SEQ ID NO:8), YPFTGPIPN (SEQ ID NO:18), SLPQNILPL (SEQ ID NO:19), TQTPVVVPPF (SEQ ID NO:20), HKEMPFPKYPVEPFTESQ (SEQ ID NO:22), and combinations thereof.

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29. [AMENDED] A method for modulating leukocyte proliferation in a patient, the method comprising administering to the patient a leukocyte regulator selected from the group of colostrinin, a constituent peptide thereof, an analog thereof, and combinations thereof, under conditions effective to change the number of leukocytes; wherein the active analog comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent structural similarity to one or more constituent peptides of colostrinin, which are selected from the group of SEQ ID NO:1 through SEQ ID NO:34.

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31. [AMENDED] The method of claim 29 wherein the leukocytes are increased in number.

32. [AMENDED] The method of claim 31 wherein the leukocytes are differentiated.

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33. [AMENDED] The method of claim 29 wherein the leukocyte regulator is a constituent peptide of colostrinin.

B7 34. [AMENDED] The method of claim 33 wherein the leukocyte regulator is selected from the group of MQPPPLP (SEQ ID NO:1), LQTPQPLLQVMMEPQGD (SEQ ID NO:2), DQPPDVEKPDLPFQVQS (SEQ ID NO:3), LFFFLPVNVLP (SEQ ID NO:4), DLEMPVLPVEPFPPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), LKPFKPKLKEVFPPF (SEQ ID NO:8), VVMEV (SEQ ID NO:9), SEQP (SEQ ID NO:10), DKE (SEQ ID NO:11), FPPPK (SEQ ID NO:12), DSQPPV (SEQ ID NO:13), DPPPPQS (SEQ ID NO:14), SEEMP (SEQ ID NO:15), KYKLQPE (SEQ ID NO:16), VLPPNVG (SEQ ID NO:17), VYPFTGPIPN (SEQ ID NO:18), SLPQNILPL (SEQ ID NO:19), TQTPVVVPPF (SEQ ID NO:20), LQPEIMGVPKVKETMVPK (SEQ ID NO:21), HKEMPFKYPVEPFTESQ (SEQ ID NO:22), SLTLTDVEKLHLPLPLVQ (SEQ ID NO:23), SWMHQPP (SEQ ID NO:24), QLPPTVMFP (SEQ ID NO:25), PQSVLS (SEQ ID NO:26), LSQPKVLPVPQKAVPQRDMPIQ (SEQ ID NO:27), AFLLYQE (SEQ ID NO:28), RGPFPILV (SEQ ID NO:29), ATFNRYQDDHGEEILKSL (SEQ ID NO:30), VESYVPLFP (SEQ ID NO:31), FLLYQEPVLGPVR (SEQ ID NO:32), LNF (SEQ ID NO:33), and MHQPPQPLPPTVMFP (SEQ ID NO:34), an active analog thereof, and combinations thereof; wherein the active analog comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent structural similarity to one or more constituent peptides of colostrinin, which are selected from the group of SEQ ID NO:1 through SEQ ID NO:34.

35. [AMENDED] The method of claim 34 wherein the leukocyte regulator is selected from the group of MQPPPLP (SEQ ID NO:1), LQTPQPLLQVMMEPQGD (SEQ ID NO:2), DQPPDVEKPDLPFQVQS (SEQ ID NO:3), LFFFLPVNVLP (SEQ ID NO:4), DLEMPVLPVEPFPPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), LKPFKPKLKEVFPEP (SEQ ID NO:8), VYPFTGPIPN (SEQ ID NO:18), SLPQNILPL (SEQ ID NO:19), TQTPVVVPPF (SEQ ID NO:20), HKEMPFKYPVEPFTESQ (SEQ ID NO:22), and combinations thereof.

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37. [NEW] A method of inducing a cytokine in a cell, the method comprising contacting the cell with an immunological regulator under conditions effective to induce a cytokine, wherein the immunological regulator is a constituent peptide of colostrinin selected from the group consisting of LQTPQPLLQVMMEPQGD (SEQ ID NO:2), DQPPDVEKPDLPFQVQS (SEQ ID NO:3), LFFFLPVNVLP (SEQ ID NO:4), DLEMPVLPVEPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPQETVT (SEQ ID NO:7), LKPFPKLKVEVFPFP (SEQ ID NO:8), VVMEV (SEQ ID NO:9), SEQP (SEQ ID NO:10), DKE (SEQ ID NO:11), FPPPK (SEQ ID NO:12), DSQPPV (SEQ ID NO:13), DPPPQS (SEQ ID NO:14), SEEMP (SEQ ID NO:15), KYKLQPE (SEQ ID NO:16), VLPPNVG (SEQ ID NO:17), VYPFTGPIPN (SEQ ID NO:18), SLPQNILPL (SEQ ID NO:19), TQTPVVVPPF (SEQ ID NO:20), LQPEIMGVPKVKETMVPK (SEQ ID NO:21), HKEMPFKYPVEPFOTESQ (SEQ ID NO:22), SLTLTDVEKLHLPLPLVQ (SEQ ID NO:23), SWMHQPP (SEQ ID NO:24), QPLPPTVMFP (SEQ ID NO:25), PQSVLS (SEQ ID NO:26), LSQPKVLPVPQKAVPQRDMPIQ (SEQ ID NO:27), AFLLYQE (SEQ ID NO:28), RGPFPILV (SEQ ID NO:29), ATFNRYQDDHGEEILKSL (SEQ ID NO:30), FLLYQEPVLGPVR (SEQ ID NO:32), LNF (SEQ ID NO:33), and MHQPPQPLPPTVMFP (SEQ ID NO:34), an active analog thereof, and combinations thereof, wherein the active analog comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent structural similarity to one or more a constituent peptides of colostrinin which are selected from the group of SEQ ID NO:2-30 and 32-34.

38. [NEW] A method for modulating an immune response in a cell, the method comprising contacting the cell with an immunological regulator under conditions effective to induce a cytokine, wherein the immunological regulator is a constituent peptide of colostrinin selected from the group consisting of LQTPQPLLQVMMEPQGD (SEQ ID NO:2), DQPPDVEKPDLPFQVQS (SEQ ID NO:3), LFFFLPVNVLP (SEQ ID NO:4),

B8 DLEMPVLPVEPFPPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), LKPFPKLKVEVFPFP (SEQ ID NO:8), VVMEV (SEQ ID NO:9), SEQP (SEQ ID NO:10), DKE (SEQ ID NO:11), FPPPK (SEQ ID NO:12), DSQPPV (SEQ ID NO:13), DPPPPQS (SEQ ID NO:14), SEEMP (SEQ ID NO:15), KYKLQPE (SEQ ID NO:16), VLPPNVG (SEQ ID NO:17), VYPFTGPIPN (SEQ ID NO:18), SLPQNILPL (SEQ ID NO:19), TQTPVVVPPF (SEQ ID NO:20), LQPEIMGVPKVKETMVPK (SEQ ID NO:21), HKEMPFPKYPVEPFTESQ (SEQ ID NO:22), SLTLTDVEKLHLPLPLVQ (SEQ ID NO:23), SWMHQPP (SEQ ID NO:24), QLPPTVMFP (SEQ ID NO:25), PQSVLS (SEQ ID NO:26), LSQPKVLPVPQKAVPQRDMPIQ (SEQ ID NO:27), AFLLYQE (SEQ ID NO:28), RGPFPILV (SEQ ID NO:29), ATFNRYQDDHGEEILKSL (SEQ ID NO:30), FLLYQEPVLGPVR (SEQ ID NO:32), LNF (SEQ ID NO:33), and MHQPPQPLPPTVMFP (SEQ ID NO:34), an active analog thereof, and combinations thereof, wherein the active analog comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent structural similarity to one or more constituent peptides of colostrinin which are selected from the group of SEQ ID NO:2-30 and 32-34.

39. [NEW] A method for modulating an immune response in a patient, the method comprising administering to the patient an immunological regulator under conditions effective to induce a cytokine, wherein the immunological regulator is a constituent peptide of colostrinin selected from the group consisting of LQTPQPLLQVMMEPQGD (SEQ ID NO:2), DQPPDVEKPDLPFQVQS (SEQ ID NO:3), LFFFLPVNVLP (SEQ ID NO:4), DLEMPVLPVEPFPPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), LKPFPKLKVEVFPFP (SEQ ID NO:8), VVMEV (SEQ ID NO:9), SEQP (SEQ ID NO:10), DKE (SEQ ID NO:11), FPPPK (SEQ ID NO:12), DSQPPV (SEQ ID NO:13), DPPPPQS (SEQ ID NO:14), SEEMP (SEQ ID NO:15), KYKLQPE (SEQ ID NO:16), VLPPNVG (SEQ ID NO:17), VYPFTGPIPN (SEQ ID NO:18), SLPQNILPL (SEQ ID NO:19), TQTPVVVPPF (SEQ ID NO:20), LQPEIMGVPKVKETMVPK (SEQ ID

**Amendment and Response**

Page 10 of 13

Serial No.: 09/641,801

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NO:21), HKEMPFPKYPVEPFOTESQ (SEQ ID NO:22), SLTLTDVEKLHLPLPLVQ (SEQ ID  
NO:23), SWMHQPP (SEQ ID NO:24), QPLPPTVMFP (SEQ ID NO:25), PQSVLS (SEQ ID  
NO:26), LSQPKVLPVPQKAVPQRDMPIQ (SEQ ID NO:27), AFLLYQE (SEQ ID NO:28),  
RGFPILV (SEQ ID NO:29), ATFNRYQDDHGEEILKSL (SEQ ID NO:30),  
FLLYQEPVLGPVR (SEQ ID NO:32), LNF (SEQ ID NO:33), and MHQPPQPLPPTVMFP  
(SEQ ID NO:34), an active analog thereof, and combinations thereof, wherein the active analog  
comprises a peptide having an amino acid sequence with at least about 15 percent proline and  
having at least about 70 percent structural similarity to one or more constituent peptides of  
colostrinin which are selected from the group of SEQ ID NO:2-30 and 32-34.

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